

# Intraosseous verrucous carcinoma arising from an orthokeratinized odontogenic keratocyst: A report of a rarest entity

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## Abstract

Intraosseous verrucous carcinomas (VCs) arising from odontogenic cysts are a rare entity. An unusual case of a VC arising from the orthokeratinized odontogenic cyst is described for the first time. The microscopic features of the lesion are presented.

**Keywords:** Epithelial cells of Malassez, odontogenic keratocyst, verrucous carcinoma, verrucous proliferation

## Introduction

Carcinomas vis-a-vis squamous cell and verrucous arising from the epithelial lining of the odontogenic cysts are rare.<sup>[1,2]</sup> Although cases of squamous cell carcinomas (SCCs) arising from the inflammatory (periapical or residual), developmental (dentigerous and keratocyst) odontogenic cysts have been documented in the world literature,<sup>[1]</sup> cases of verrucous carcinoma (VC) arising from the odontogenic keratocyst are extremely rare.

VC represents 1–10% of all the oral SCCs, is predominantly seen in the older men in the mandibular vestibule, buccal mucosa, and hard palate.<sup>[3]</sup> VCs are described as slow-growing, exophytic, lesions with indolent clinical course and a potential for local recurrence. Primary intraosseous VC (IOVC) arising from an odontogenic cyst is an extremely rare lesion.<sup>[3]</sup> To our knowledge, only one case of VC occurring in the parakeratinized odontogenic keratocyst (keratocystic odontogenic tumor) has been reported in literature.<sup>[3]</sup> We herein report the first case of IOVC arising from an orthokeratinized odontogenic keratocyst.

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## Case Report and Results

A 64-year-old male with a history of tobacco smoking reported to the Department of Oral Medicine and Radiology for the evaluation of 1-year-old painful swelling on the left maxillary alveolus [Figure 1a]. Past history revealed the extraction of maxillary teeth (22, 23, and 24) 2 years back. After one year of extraction, he developed pain and swelling in that region. On inspection, the overall surface of the swelling was smooth, but some areas showed finger-like proliferations with central areas of necrotic tissue [Figure 1b]. The lesion was firm and tender on palpation. Further, the radiographic investigation revealed a well-defined radiolucency measuring 20 mm × 28 mm which was extending from the distal aspects of the left maxillary central incisor to second premolar region [Figure 2]. Axial and coronal sections of the cone-beam computed tomography imaging depicted a large expansile radiolucency involving the maxillary process with thinning of the cortical bone [Figure 3a, b]. Looking into the clinical and radiological features, we considered two separate entities, i.e. residual cyst and proliferative verrucous leukoplakia.

## Histological findings

Incisional biopsy was performed from the buccal alveolar region (canine region) and sent for histopathological diagnosis. The hematoxylin- and eosin-stained sections of the received specimen showed cystic lining made up of orthokeratinized, relatively thin stratified squamous epithelium of uniform thickness without evidence of rete ridges, with prominent keratohyaline granules in the superficial layers. The basal layer cells were cuboidal and hyperchromatic and did not

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demonstrate palisading. The epithelial lining was detached from the underlying connective tissue capsule, which was fibrocellular and showed moderately intense chronic inflammatory cell infiltrate. These features were suggestive of an orthokeratinized odontogenic cyst; however, at the focal area, the cystic lining showed hyperplasia and few verrucous projections [Figure 4a and b]. Hence, the true diagnosis was not possible with the incisional biopsy, and so, excisional biopsy was performed.

Intraoperatively, the cystic lesion was found in the maxilla. The enucleated cyst lining along with the extracted teeth 21 and 25 was resubmitted for histopathological examination. Macroscopically, the enucleated cystic lining was continuous with the exophytic proliferation seen on the palatal surface and also demonstrated numerous verrucous projections on the luminal surface of cystic lining [Figure 5a and b]. The tissue was harvested from the received large specimen and was subjected to routine tissue processing. Upon hematoxylin and eosin staining, the sections showed findings similar to those of the previous biopsy in most parts of the cyst wall, suggestive of an orthokeratinized odontogenic cyst. Furthermore, this cystic lining was in continuum with areas showing wide and elongated, broad rete ridges appearing to push into the underlying fibrocellular connective tissue stroma. The surface of the epithelium in these areas showed exophytic/verrucous projections lined by parakeratin and formed clefts with parakeratin plugging. Mild cellular atypia and koilocytes were evident. Desquamated keratin was seen within the cyst lumen. The subepithelial connective tissue stroma showed intense lymphocytic infiltrate. Based on the histopathology of both incisional [Figure 4a and b] and excisional biopsies [Figures 6-8], the diagnosis of IOVC arising from an orthokeratinizing odontogenic cyst was made. Postoperative healing was uneventful with no signs of recurrence after 6 months of recall visit.

## Discussion

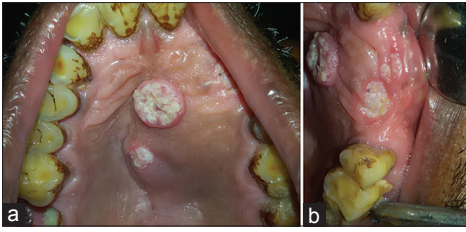
An occurrence of a cyst and an adjoining carcinoma (although unrelated to VC, may well be applied to this condition also) in the jaws is open to numerous versions. Ward and Cohen<sup>[4]</sup> pointed out three possible explanations: (1) A pre-existing cyst becomes secondarily involved in a carcinoma of unrelated origin arising either from an adjacent epithelial structure or as a metastasis from a distant primary tumor; (2) the lesion is a carcinoma from the outset, a part of which has undergone cystic transformation; or (3) the initial lesion is a cyst, and malignant change has subsequently taken place in the epithelial lining. The only unquestionable proof that a carcinoma has arisen in an odontogenic cyst is the histologic demonstration of a transition of the cells lining the cyst from a benign epithelium to a carcinoma,<sup>[1,5-7]</sup> which was well appreciated in the current case. Cystic transformation of a carcinoma was excluded because both the initial biopsy and most parts of the enucleated specimen showed a benign

epithelial lining. The possibilities of verrucous carcinomatous transformation of the epithelial lining of a cyst or fusion of a cyst and mucosal VC can be considered. However, considering the gross pathology of the lesion, which showed keratotic, verrucous projections on the luminal surface and the histopathological feature of the contiguous relationship of the cystic lining with the verrucous carcinomatous region, the development of mucosal VC with secondary involvement of the cyst lining was a less likely possibility. In addition, histologically, the cystic lining was contiguous with the epithelium which was composed of alternating areas of ortho- and para-keratinized stratified squamous epithelium, proliferating at areas. This lining was in continuum with areas showing wide and elongated, broad rete ridges appearing to push into the underlying fibrocellular connective tissue stroma. The surface of the epithelium in these areas showed exophytic/verrucous projections lined by parakeratin and formed clefts with parakeratin plugging. Mild cellular atypia and koilocytes were evident. Desquamated keratin was seen within the cyst lumen. The subepithelial connective tissue stroma showed intense lymphocytic infiltrate. Based on the histopathology of both incisional and excisional biopsies, the diagnosis of IOVC arising from an orthokeratinizing odontogenic cyst was made [Figures 6 and 7b-d].

There was no preoperative evidence that this lesion was initially VC which began on the mucosal surface and then extended into the bone. Further, the lesion had many of the characteristic features of a large odontogenic cyst, with the exception of some buccal cortical plate erosion and palatal perforation (automarsupialized?) of short duration leading to the discharge of a keratinaceous material; the lesion was contained in a well-defined, unilocular, gnathic bone cavity. Hence, given the clinical as well as radiographic presentation, gross appearance, and microscopy of the specimen, the diagnosis of IOVC arising from an orthokeratinized odontogenic cyst was made.

Verrucous proliferation and VC can be distinguished by the observation that the hyperplastic epithelium of the verrucous processes remains superficial to the adjacent normal epithelium; while in VC, the broad rete processes extend deeper than the abutting normal epithelium and often envelopes a margin of normal epithelium into the underlying connective tissue.<sup>[2]</sup> The broad rete processes extending deeper than the abutting normal epithelium were clearly evident in the present case, and hence considered it as VC.

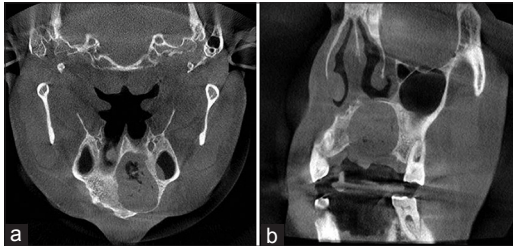
Although an orthokeratinized keratocyst has been clinically considered to be less aggressive than a parakeratinized variant, it has been suggested that the earlier variant may be at a greater risk for malignant transformation.<sup>[1]</sup> SCC orthokeratinized odontogenic cyst has been well documented in literature;<sup>[8]</sup> however, IOVC arising from an orthokeratinized odontogenic cyst is being reported for the first time.



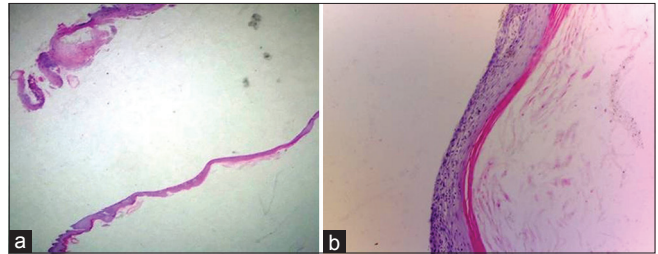
**Figure 1:** (a and b) Clinical photograph showing a unilateral swelling on the left hard palate and alveolus with multiple papillary exophytic growths



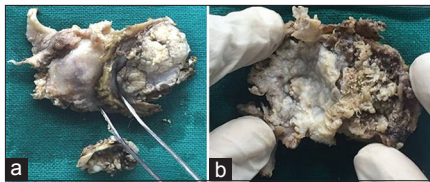
**Figure 2:** Panoramic view showing a unilocular radiolucent lesion extending from the distal aspect of tooth 21 to the mesial aspect of tooth 25



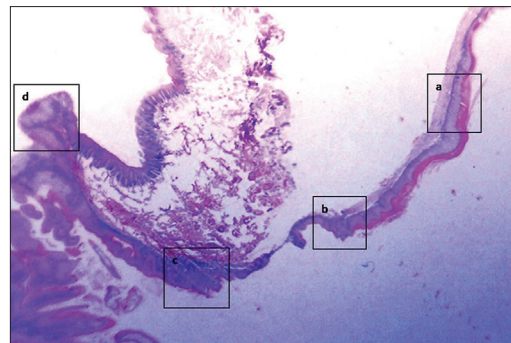
**Figure 3:** (a and b) Axial and coronal sections of the cone-beam computed tomography imaging showing a large expansile radiolucency involving the maxillary process with thinning of the cortical bone



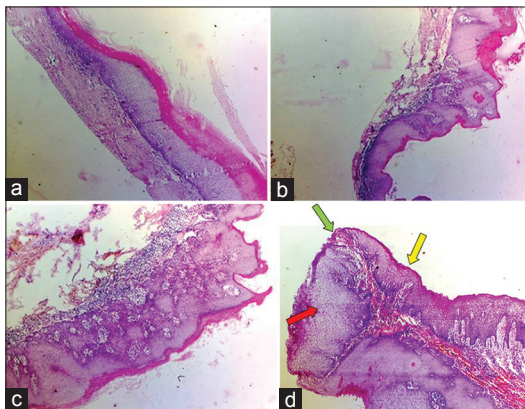
**Figure 4:** (a) Stereomicroscopic photomicrograph of the cystic lining of the incisional biopsy specimen showing few verrucous projections at focal area and separation from the connective tissue capsule, and (b) magnified view of Figure 4a showing thin, flattened, orthokeratotic lining with hyperchromatic basal layer and keratohyaline granules (H and E,  $\times 100$ )



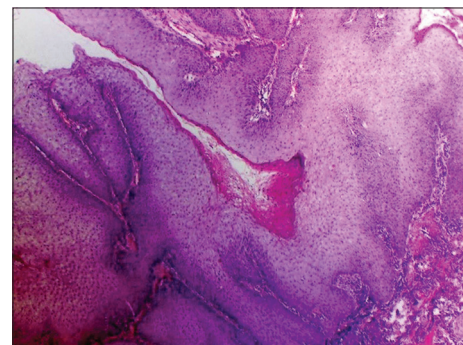
**Figure 5:** (a) Gross picture of the enucleated cyst lining which is continuous with the exophytic proliferation seen on the palatal surface, (b) numerous verrucous projections on the luminal surface of cystic lining



**Figure 6:** Stereomicroscopic view of H- and E-stained section of the lesion



**Figure 7:** (a) Higher magnification of the framed area (a) in Figure 6 showing cystic lining which is similar to the incisional biopsy findings (H and E,  $\times 100$ ), (b and c) higher magnification of the framed areas (b) and (c) in Figure 6 showing blunt rete ridge formation and verrucous transformation in cystic lining (H and E,  $\times 100$ ), (d) higher magnification of the framed area (d) in Figure 6 showing unaltered masticatory mucosa of the hard palate (yellow arrow), cystic epithelium having broad rete ridges appearing to push into the underlying connective tissue stroma (red arrow) and impervious junction of both the epithelium (green arrow) (H and E,  $\times 100$ )



**Figure 8:** Photomicrograph of the section from another area of the cystic lining showing marked epithelial hyperplasia having clefts filled with parakeratin plugging and broad, pushing, blunt rete ridges without a significant dysplasia (H and E,  $\times 100$ )

**Table 1: Reported cases of VP and VC arising in odontogenic cysts**

Author	Age	Sex	Site	Presenting feature	Diagnosis
Enriquez (1980) <sup>[10]</sup>	56 yr	M	Mandible	Painless mass with draining fistula	VC arising in an odontogenic cyst (NS)
Pomatto et al (2001) <sup>[9]</sup>	NA	NA	Maxilla	NA	VC arising from an infected dentigerous cyst
Aldred et al (2002) <sup>[11]</sup>	13 yr	F	Maxilla	Swelling on the right maxillary alveolus	Odontogenic Cyst(NS) With VP
Ueek et al (2007) <sup>[2]</sup>	46 yr	M	Mandible	Swelling, paresthesia	Keratinizing Odontogenic Cyst(NS) With VP
Mohtasham et al (2008) <sup>[3]</sup>	58 yr	M	Maxilla	Firm, nontender, white-pink, exophytic polypoid lesion	IOVC originating from an odontogenic cyst (NS)
Imaue et al (2013) <sup>[12]</sup>	NA	NA	Maxilla	Painless exophytic lesion	VC originating from a previous cyst (NS)
Argyris et al (2015) <sup>[13]</sup>	32	M	Mandible	Painless swelling	keratinizing Odontogenic Cyst (NS) with verrucous hyperplasia and epithelial dysplasia
Peng et al (2015) <sup>[14]</sup>	74	M	Mandible	Swelling with pus discharge	IOVC arising from an infected dentigerous cyst
Present case	65	M	Maxilla	Swelling	IOVC from orthokeratinized OKC

VC: Verrucous carcinoma, NS: (Variant) Not specified, NA: Not available, VP: Verrucous proliferations, IOVC: Intraosseous verrucous carcinoma

Primary intraosseous carcinoma is an extremely rare lesion, almost always occurring in cranial bones. The origin of this tumor, specific to the maxillae, is associated with the cells of the epithelial rests of Malassez.<sup>[9]</sup> Cases of odontogenic cysts with either verrucous changes or VC in the lining published so far in literature have been shown in Table 1.

We consider this unusual case as the first case of IOVC arising from an orthokeratinized odontogenic cyst. One would have to speculate about its pathogenesis. Its position provides an evidence for an odontogenic origin. Although viral etiology has been implicated for the epithelial proliferation leading to verrucous configuration, immunocytochemical staining and polymerase chain reaction amplification for viral DNA did not support the evidence of viral etiology.<sup>[11,13]</sup> The presence of hypergranulosis and cells resembling koilocytes though suggested the possibility of human papillomavirus (HPV) involvement in our case, technical and economical limitations failed to permit the analysis of HPV DNA in the cyst lining.

## Conclusion

Owing to the scarcity of such lesions, clinicians who may encounter future cases must be aware that VC could occur in the wall of odontogenic cysts and tumors, and the clinical behavior of such lesions till date remains largely unknown. Hence, considering the rarity of the similar reported lesions, close clinical and radiographic follow-up of such lesions is recommended.

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## Conflicts of interest

There are no conflicts of interest.

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